

10, line 28 to recite "initiating methionine." This amendment corrects an inadvertent typographical error.

None of the amendments constitutes new matter. Their entry is requested.

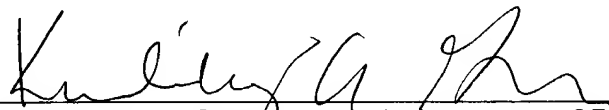
THE OFFICE ACTION

The Examiner states that page 32, lines 14, 15, 18 and 19 of the specification contains sequence disclosures that are encompassed by the definitions for nucleotides and/or amino acid sequences set forth in 37 C.F.R. §§ 1.821(a)(1) and 1.821(a)(2). The Examiner states that reference must be made to the sequences by use of an assigned identifier in the text of the description or claims of the application.

Pursuant to 37 C.F.R. §§ 1.825(a) and (b), applicant has provided herewith a substitute Sequence Listing, which provides SEQ ID NOs for the nucleic acid sequences disclosed on page 32, lines 14-19 of the specification. Applicant has also amended the substitute Sequence Listing to reflect the SEQ ID NOs for the amino acid sequences described on page 9, lines 13-19 and page 10, lines 25-30 of the specification and shown in Figure 1 and Figure 5, respectively. Applicant has also amended the Sequence Listing to update the application information section to recite the current application number, filing date and the priority application numbers and filing dates.

Accordingly, applicant submits herewith a paper copy of a substitute Sequence Listing and a CRF copy of the substitute Sequence Listing. Applicant also submits a statement pursuant to 37 C.F.R. §§ 1.825(a) and (b) verifying that the content of the paper copy of the substitute Sequence Listing is identical to the CRF copy of the substitute Sequence Listing and that the submission of this substitute Sequence Listing does not include new matter.

Respectfully submitted,



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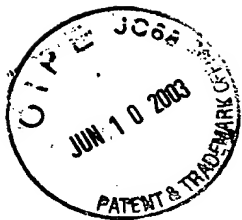
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Appendix of Amendments

Replace on page 9, lines 13-19 with the following paragraph:

Figure 1. (A) Predicted amino acid sequence of human APRIL (SEQ ID NO: 2). The predicted transmembrane region (TM, boxed), the potential N-linked glycosylation site (star) and the N-terminus of the recombinant soluble APRIL (sAPRIL) are indicated. (B) Comparison of the extracellular protein sequence of APRIL (SEQ ID NO: 6) and some members of the TNF ligand family. Identical and homologous residues are represented in black and shaded boxes, respectively. TNF α , tumor necrosis factor α (SEQ ID NO: 7), LT α , (lymphotoxin α) (SEQ ID NO: 8), FasL, (Fas (CD95) ligand) (SEQ ID NO: 9), TRAIL (SEQ ID NO: 10), TWEAK (SEQ ID NO: 11) and TRANCE (SEQ ID NO: 12), (RANK ligand).

Replace page 10, lines 25-30 with the following paragraph:

Figure 5. An alignment of the human (SEQ ID NO: 5) and mouse (SEQ ID NO: 4) APRIL amino acid sequences showing the extensive identity between the two proteins. Identical residues are marked with the overlaying dot. The underlined residues represent a potential N-linked glycosylation site. The [initiating] initiating methionine is considered a likely start site, however, it is possible

that in frame methionines further upstream may serve as the actual start site, for example, in the human sequence.

Replace page 32, lines 10-21 with the following paragraph:

In order to explore possible activities of APRIL, we expressed a recombinant form of soluble extracellular domain of APRIL (sAPRIL) encompassing amino acids 110 to 250 in 293 cells (9). The full length APRIL gene was amplified from the EST-clone, using a specific 5' forward primer flanked by a EcoRI site (5'-CCAGCCTCATCTCCTTTCTTGC-3') (SEQ ID NO: 13) and a specific 3' reverse primer flanked by an XbaI site (5'-TCACAGTTTCACAAACCCCAGG-3') (SEQ ID NO: 14). The amplified fragment was cut with EcoRI/XbaI and cloned into a modified version of pCRIII (Invitrogen), in frame with an N-terminal Flag peptide (15). The soluble form of APRIL (sAPRIL) was generated using the two primers (5'-AAACAGAAGAAGCAGCACTCTG-3') (SEQ ID NO: 15) and (5'-TCACAGTTTCACAAACCCCAGG-3') (SEQ ID NO: 16) containing a PstI and XbaI site, respectively, and subsequently cloned into a modified pCRIII vector, containing both a HA signal for protein secretion in eukaryotic cells and an N-terminal Flag epitope (15).